

REMARKS

Applicant respectfully requests reconsideration. Claims 92-130 were previously pending in this application. Claims 105, 110, 113 and 116 are canceled herewith as being drawn to a non-elected invention. Applicant notes that claim 113 is included, as Applicant believes that the subject matter of the claim is directed to a non-elected invention. Claims 92, 101, 103, 104, 106-109, 111, 112, 114, 115, 117, 118 and 128-130 have been amended for clarification purposes. The amendments are believed to not alter the scope of the claims. Support for the claim amendments can be found throughout the instant specification and in the claims as originally filed. As a result, claims 92-104, 106-109, 111, 112, 114, 115 and 117-130 are pending for examination with claims 92 and 104 being independent claims.

No new matter has been added.

Restriction Requirement

Applicant thanks the Examiner for indicating that the requirement for the election of a species of animal or protein has been withdrawn.

Information Disclosure Statement

In regard to the Examiner's objection to the listing of references in the specification as not being a proper Information Disclosure Statement, Applicant notes that the listing is not intended to constitute an Information Disclosure Statement. If necessary to do so, Applicant will submit an Information Disclosure Statement during the prosecution of this application.

Claim Objections

The Examiner has objected to claims 92 and 104 for allegedly appearing to be incomplete. According to the Examiner, the claims appear to be incomplete as the final step does not result in the intent set forth in the preamble.

Applicant respectfully disagrees. However, in the interest of expediting prosecution of this application, Applicant has amended claims 92 and 104. Applicant notes that the preamble of claim 92 recites a "method for the production of transgenic animals", and the final step (step g)) of the claim recites the step of producing the transgenic animal. The preamble of claim 104

recites a “method of preparing a genetically engineered transgenic mammal”, and the final step (step (f)) recites the step of producing the transgenic mammal.

Accordingly, withdrawal of the objections is respectfully requested.

Rejections under 35 U.S.C. §112

The Examiner rejected claims 93-104, 107-109, 111-115 and 117-130 under 35 U.S.C. §112, first paragraph, for an alleged lack of enablement. Applicant notes that the Examiner did not include independent claim 92 in this rejection.

According to the Examiner, while being enabling for a method for cloning a non-primate mammal through a nuclear transfer process using non-primate mammalian cells as a source of donor nuclei comprising an additional recloning step using a cell from a first nuclear transfer embryo, said method wherein it further comprises genetically modifying a fibroblast cell *in vitro* prior to the initial nuclear transfer, and a non-primate mammal made by the method wherein when the mammal is transgenic and the transgene is expressed, does not reasonably provide enablement for the claimed method in primate species. Applicant would like to note for the record that claim 92 and many of the claims that depend therefrom are not limited to mammals but rather are directed to animals generally.

Applicant respectfully traverses. At the time of filing, the cloning of primates had been successfully performed contrary to the Examiner’s assertions (See, e.g., Meng et al. Biol. Reprod. 1997, 2: 454 and Chan et al. Science 2001, 291: 309). Meng et al., for example, teach a method for the generation of rhesus monkeys by nuclear transfer, while Chan et al., for example, teach the production of transgenic rhesus monkeys. Applicant maintains, therefore, that a person of ordinary skill in the art could use the teachings of Meng et al. and Chan et al. in combination with the teachings of the instant specification and practice the claimed methods.

In addition, even if some embodiments of the claims were inoperable, which Applicant does not concede is in fact the case, according to MPEP 2164.08(b), the presence of inoperative embodiments within the scope of a claim does not render the claim non-enabled if one of ordinary skill in the art would be able to determine which embodiments are operative or inoperative with no more than routine experimentation. Applicant maintains that this is the case with the guidance provided in the specification and the high level of skill of one of ordinary skill

in the art. Therefore, even though the Examiner argues that primate embodiments are not enabled, this is not the standard by which enablement should be evaluated in regard to the rejected claims.

Also, according to the Examiner, the claims encompass non-enabled embodiments requiring introduction of a transgene into a differentiated, non-fibroblast somatic cell *in vitro*, prior to insertion of the donor nucleus into an enucleated oocyte. It is the Examiner's contention that the specification does not teach *in vitro* transformation of fetal or adult somatic cells immediately prior to nuclear transfer and that genetic modification of somatic cells in culture was an underdeveloped art. The Examiner further argues that the only somatic cell type that could be genetically modified in culture to form an animal was a fibroblast.

Applicant respectfully traverses. Step a) of claim 92 is directed to transfecting a first non-human differentiated somatic cell or cell-line with a transgene containing a first DNA sequence. This step is routine in the art and can be accomplished, for example, by the generation of transgenic cell lines through homologous recombination, an established molecular biology technique. While certain cell lines may be more easily transfected than others, this does not demonstrate that one of ordinary skill in the art is not enabled to perform the transfection as recited in step a) of claim 92.

Additionally, Applicant contends that with the teachings provided in the specification in combination with the knowledge in the art, one of ordinary skill would be enabled to make a transgenic animal as recited in the rejected claims and not only with fibroblast cells as argued by the Examiner. The teachings of the instant specification go beyond the use of fetal fibroblast cells and encompass somatic cells generally. The Examiner has not sufficiently demonstrated why Applicant's teachings in combination with the knowledge in the art are deficient in this regard. Further, as argued above, even if some embodiments of the claims were inoperable, which Applicant does not concede is in fact the case, the presence of inoperative embodiments within the scope of a claim does not necessarily render the claim non-enabled.

Lastly, according to the Examiner, claim 20 does not require expression of the transgene, and the specification does not teach how one of skill in the art would use a transgenic non-human mammal that does not express the transgene.

Applicant respectfully traverses. Applicant notes that claim 20 has been canceled. In addition, Applicant further notes, without conceding the correctness of the Examiner's rejection if applied to transgenic non-human animals produced by the methods of the claims, that none of the currently pending claims are directed to such animals. It is not clear how the Examiner's arguments on this basis are even relevant to the claims, which are directed to methods of producing transgenic animals. All that is required of Applicant is to teach one of ordinary skill in the art how to perform the claimed methods and how to use such methods. Even if, *arguendo*, the practice of the methods results in the generation of animals that do not express the transgene, that such animals may be produced is not the standard by which enablement of the claims should be judged.

Accordingly, withdrawal of the rejection is respectfully requested.

The Examiner has rejected claim 130 under 35 U.S.C. §112, second paragraph, as allegedly being indefinite. The Examiner has argued that the term "primary derived fibroblasts" is vague and unclear.

Applicant respectfully traverses. The term "primary-derived" is defined on page 10 of the instant specification. One of ordinary skill in the art would understand, based on this definition, that primary-derived cells, such as fibroblasts, refer to primary cells that have undergone at least one subsequent division.

Accordingly, withdrawal of the rejection is respectfully requested.

Rejections Under 35 U.S.C. §103

The Examiner has rejected claims 93-104, 106-109, 111-115 and 117-130 under 35 U.S.C. §103(a) as allegedly being unpatentable over Schnieke (1997, Science, 278: 2130-2133), Wilmut (1997), Campbell (1996), Campbell (1994, Biology of Reproduction 50:1385-1393) in view of Zakhartchenko (1999) and Wells (1999). Applicant notes that claim 92 was not included in this rejection.

According to the Examiner, the claims are drawn to a method of cloning a non-human mammal comprising transferring the nucleus of a differentiated mammalian cell into an enucleated oocyte of the same species, simultaneously activating the resulting cell couplet,

culturing the embryo until it reaches at least the two-cell stage and using a cell from said embryo to form a second embryo through a second round of nuclear transfer. Further, according to the Examiner, Schnieke teaches all the elements of the claims, except for the recloning step as required by step (vii) of claim 1 and that Zakhartchenko et al. and Wells et al. each teach using a recloning step.

Applicant respectfully traverses. It seems that the rejection of the Examiner does not pertain to the pending claims as the claims do not refer to “simultaneously activating the resulting cell couplet, culturing the embryo until it reaches at least the two-cell stage and using a cell from said embryo to form a second embryo through a second round of nuclear transfer”. In addition, Applicant notes that claim 1 has been canceled. In addition, Applicant notes that the Zakhartchenko (1999) and Wells (1999) are not properly included in this rejection. The instant application has a priority date of November 2, 1998, while the Zakhartchenko and Wells references were published in 1999.

Further, even if the references could be applied, the teachings of the cited references alone or in combination do not add up to the claimed invention. None of the references teach, at least, performing a first round of nuclear transfer to generate a first transgenic animal and performing a biopsy on the animal and characterizing cells derived from the animal or using the differentiated somatic cells from the animal generated through the first nuclear transfer to perform a second round of nuclear transfer. Zakhartchenko et al. and Wells et al. merely teach recloning from blastomeres obtained from 5 day old morulae. The second round of transfer is not performed with differentiated somatic cells that have been characterized, as claimed.

Accordingly, withdrawal of the rejection is respectfully requested.

The Examiner has rejected claims 93-104, 107-109, 111-115 and 117-130 under 35 U.S.C. §103(a) as allegedly being unpatentable over Schnieke (1997, Science, 278: 2130-2133), Wilmut (1997), Campbell (1996), Campbell (1994, Biology of Reproduction 50:1385-1393) in view of Zakhartchenko (1999) or Wells (1999), and further in view of Campbell (WO 00/42174 published July 20, 2000). Again, Applicant notes that claim 92 was not included in this rejection.

Applicant respectfully traverses. As argued above, it is unclear to Applicant if the Examiner based the rejection on claims that are currently pending or on claims that have been canceled. Applicant notes that the Examiner, as part of this rejection, refers to claims 1, 2, 5-9, 11, 13, 17, 19, 20 and 22, which are not currently pending. In addition, similar to above, Applicant notes that the Zakhartchenko (1999), Wells (1999) and Campbell (WO 00/42174 published July 20, 2000) are not properly applied. The instant application has a priority date of November 2, 1998, while these references were published after Applicant's priority date. Finally, also as argued above, even if the references could be applied, the teachings of the cited references alone or in combination do not add up to the current claimed invention. Reasons that support Applicant's contention are provided in response to the above rejection and are reiterated here by reference.

Accordingly, withdrawal of the rejection is respectfully requested.

CONCLUSION

A Notice of Allowance is respectfully requested. The Examiner is requested to call the undersigned at the telephone number listed below if this communication does not place the case in condition for allowance.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, that is not covered by an enclosed check, please charge any deficiency to Deposit Account No. 23/2825.

Respectfully submitted,
Echelard et al., Applicant(s)

By:



Janice A Vatland, Ph.D.
Reg. No.: 52,318
Wolf, Greenfield & Sacks, P.C.
600 Atlantic Avenue
Boston, Massachusetts 02210-2206
Telephone: (617) 646-8000

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